



## Early Journal Content on JSTOR, Free to Anyone in the World

This article is one of nearly 500,000 scholarly works digitized and made freely available to everyone in the world by JSTOR.

Known as the Early Journal Content, this set of works include research articles, news, letters, and other writings published in more than 200 of the oldest leading academic journals. The works date from the mid-seventeenth to the early twentieth centuries.

We encourage people to read and share the Early Journal Content openly and to tell others that this resource exists. People may post this content online or redistribute in any way for non-commercial purposes.

Read more about Early Journal Content at <http://about.jstor.org/participate-jstor/individuals/early-journal-content>.

JSTOR is a digital library of academic journals, books, and primary source objects. JSTOR helps people discover, use, and build upon a wide range of content through a powerful research and teaching platform, and preserves this content for future generations. JSTOR is part of ITHAKA, a not-for-profit organization that also includes Ithaka S+R and Portico. For more information about JSTOR, please contact [support@jstor.org](mailto:support@jstor.org).

## SOME OBSERVATIONS UPON OPSONINS IN PNEUMONIA AND IN FOUR STREPTOCOCCUS INFECTIONS.\*

NATHANIEL BOWDITCH POTTER, M. D.

Visiting Physician to the French Hospital, New York

AND

CHARLES KRUMWIEDE, M. D.

Assistant Pathologist to the French Hospital, New York

### METHOD.

THE technique was essentially that of Wright and Douglas. The bacterial emulsion was at first prepared by mixing the growth from agar in NaCl solution, and for the observations upon streptococci this method was adhered to on account of the necessity for thoroughly breaking up the chains; but for pneumococci, a 24-hour broth culture was found to furnish an emulsion of just the right thickness. A meat-extract broth, reaction + 1 per cent, gave constant results.

The smears were made with cigarette paper. This gave an even distribution (mainly along the edge), and caused little trauma to the leucocytes. In staining, trials were made to find a method which would stain the leucocyte so that its margins were sharp as shown by granulations, yet which would stain the organisms deeper than the nucleus, so that they could be readily seen when near or overlying the latter. For pus cocci we found that due to their great affinity for methylene blue, a few seconds' staining in Jenner gave excellent results. Pneumococci, however, were too faintly stained. When the slide was flooded with J. Homer Wright's stain for one to two minutes, rinsed, and counterstained with methylene azure for 10 to 20 seconds, the nucleus was reddish and the cocci deep purple.

About 25 sera were tried, using the usual Wright-Douglas method with the above additions. The sera were normal and from pneumonia patients; usually three samples were taken from each person. The source was unknown until after the estimations were made. Duplicate preparations were also made from one tube. The time of incubation was varied, 10 minutes giving the best results for pneumococci. With a longer time the cocci stained less sharply and

\* Received for publication June 15, 1907.

intensely and were therefore difficult to count. The degree of accuracy was not very satisfactory; occasional figures showed 33 per cent or more difference, many 18 to 22 per cent, though in more than half the difference was much smaller. Counting 200 cells corrected such differences but slightly. It was noticed that the laboratory temperature made a decided difference in the degree of phagocytosis which was much lower on cold days. Warmed solutions were then employed. The pipettes were then calibrated so that equal quantities were used through one series. A system of counting the doubtful cells and cocci was then strictly adhered to, one point being to ignore packed leucocytes as accidental, another only to count isolated leucocytes, avoiding even the smaller clumps. Thorough mixing of the cream prevented most of such clumping. Adherence to these details diminished the variations materially. At least 10 per cent variation in the opsonic index may be due to the sources of error in the method and cannot be considered. Often the error may be more. The variations in using two sets of leucocytes are given later.

#### LOBAR PNEUMONIA.

*Three fatal cases.*—E. H., died of acute cardiac dilatation on 7th day. On 6th day, good condition, lower left lobe consolidated. Leucocytes 21,000. Opsonic index 0.96.

J. S., died with toxemia and hyperpyrexia. Just before death, leucocytes 11,000; polynuclears 73 per cent. Opsonic index 1.16.

J. M., spreading pneumonia, death 15th day, edema of lungs. On 10th day, leucocytes 15,000, polynuclears 88.5 per cent. Opsonic index 0.95. On 14th day, leucocytes 13,600, polynuclears 88 per cent. Opsonic index 0.89.

*Four cases with crisis.*—The opsonic index rose on the day of crisis, was highest the day after crisis, and fell within a few days to normal, the leucocytes and polynuclears falling. One case showed the following: On the sixth day in hospital a pseudo-crisis occurred, leucocytes 8,500, polynuclears 81.5 per cent. Opsonic index, 1.63. The temperature again rose, a second critical fall on 8th day, leucocytes 11,800, polynuclears 68 per cent. Opsonic index, 1.53.

*Three cases with lysis.*—One case showed a moderate rise during lysis to 1.29. A mild case showed no change. The third case already convalescent showed no change.

*Two cases terminating with empyema.*—One showed a beginning rise when resolution took place. The opsonic index was 1.50, 10 days later. One week later when pus was forming, it was still 1.33. Another case showed no rise.

#### BRONCHO-PNEUMONIA.

Isolated observations on two cases during fall of temperature showed a slight rise, to 1.25 in one case.

All opsonic indices taken during the course of the disease (except the one with pseudo-crisis) were approximately normal or slightly below.

## STREPTOCOCCUS INFECTIONS.

*Case 1.*—J. M. B. Male. 30. Dr. S. W. Lambert. Entered New York Hospital October 22, 1906. Septicemia, ulcerative endocarditis; double pleurisy with effusion. Blood cultures gave *Strept. tenuis*. Leucocytes 10,000 to 12,000. Septic temperature 99° to 103°. Opsonic index to streptococcus from blood October 31, 0.46. Died November 2, before vaccine was completed. Not inoculated.

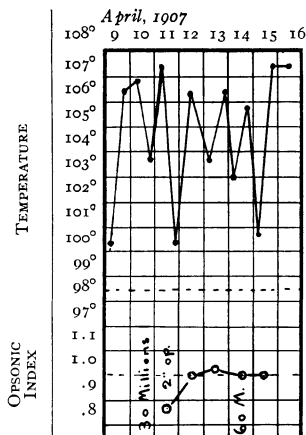
*Case 2.*—M. V. Female. 23. Seen with Dr. W. S. Bryant, April 10, 1907, at French Hospital. History of cold for seven days, earache for three days. Right mastoid operation April 5. Blood culture: streptococcus (by Dr. Krumwiede). Extensive otitis. Very little pus. April 6, wound sloughed. April 7 and 8, dressed with horse serum, sloughing stopped. April 10, inoculated with 30 millions streptococci (A. R.), Case 3 below. April 11, second operation, excision of right internal jugular, curettage of lateral sinus. April 15, inoculated with 60 millions streptococci (A. R.). Became delirious. Metastases in left shoulder and right wrist. April 16, died. Autopsy showed meningitis.

Result of inoculation: no appreciable effect upon clinical condition nor upon opsonic index which remained normal. (See chart.)

CHART I.

M. V. STREPTOCOCCUS SEPTICEMIA, MENINGITIS.

Inoculated with streptococcus from A. R.



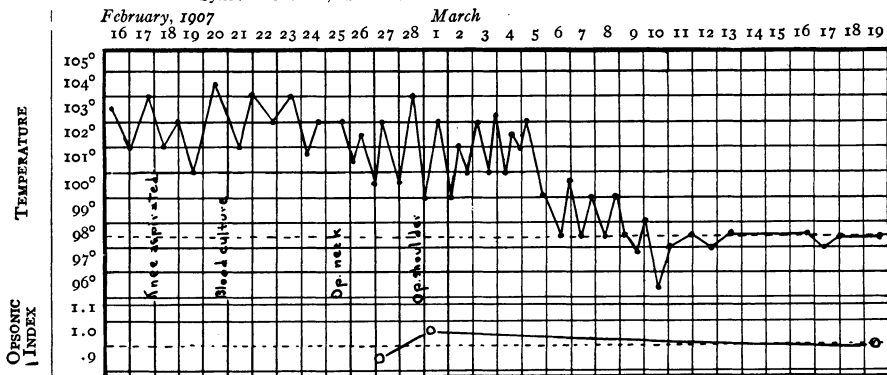
*Case 3.*—A. R. Male. 20. Entered French Hospital February 15, 1907. No antecedent sore throat, venereal, or other illness. Four or five days before admission, pain in left shoulder, indigestion, vomiting, diarrhea. Three days before, pain in right knee, fever. Two days before, slight nose bleed and chilly feelings.

Physical examination: Cyanotic, flushed cheeks, eyes bright. Injected conjunctivae. Lips dry, heavily coated tongue. Swelling with edema, above and to the inside of the left shoulder joint, and over lower part of neck. Left arm held immobile. Attempt at motion apparently very painful, resisted by patient. Right knee enlarged,

tender; fluid in joint. Abdomen tympanitic. Spleen palpable, just below costal margin, soft. Liver, slightly enlarged, edge palpable. Nothing abnormal in rectum. No discharge from urethra. February 17, slight epitaxis. February 18, tongue dry, thickly coated, yellowish brown. Glands enlarged behind left sternocleidomastoid. Marked induration about shoulder, some little redness, heat, the edema has extended behind anterior edge of trapezius and to margin of sternum. Knee aspirated, 5 c.c. cloudy fluid: *Strept. pyogenes*. Delirious in evening, restless sleep. Liquids. February 19, faint soft systolic murmur heard at base and apex. Induration increased beneath left sternocleidomastoid. Right femoral and inguinal glands enlarged; rather soft. Femoral tender. Urine: amber, slightly cloudy, albumen trace, no sugar, few epithelial cells and leucocytes. February 20, slight conjunctival icterus. Edema about shoulder has extended slightly and is more brawny. Tongue cleaner. Patient rather somnolent. Catheterized. February 21, less somnolent. Pulse bounding. Urine: gave faint trace

CHART 2.  
A. R. STREPTOCOCCUS SEPTICEMIA.

Synovitis of knee, abscess of neck and of shoulder. Not inoculated.

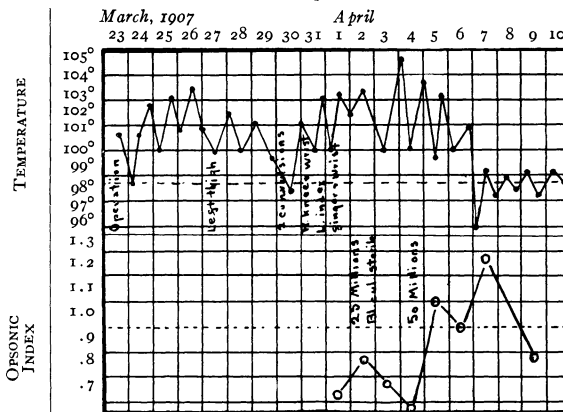


of albumen. Sediment as above. Blood culture: *Strept. pyogenes* (Dr. Krumwiede). February 22, slight nose bleed. Has slept better than any night. Much less restless. February 24, attempt was made to determine patient's opsonic index to streptococcus from his blood. No phagocytosis occurred. February 25, profuse perspiration. Vomited yellow curds. February 26, softening and localization behind sternocleidomastoid. Abscess opened under cocaine by Dr. Peck. Few drops of yellow pus, drained. Culture: *Strept. pyogenes*. February 27, several wheals on trunk. February 28, second attempt to determine patient's opsonic index successful. March 1, free perspiration at night. Urine: dark amber, few granular casts. March 2, Abscess about shoulder opened. Culture: *Strept. pyogenes*. March 3, patient's general condition continues the same. Involuntary micturition. Soft diet. March 5, vaccine prepared but its use delayed because patient's general condition had slightly improved. March 6, urine: no casts. March 9, wheals have gradually disappeared. Knee has gradually diminished in size, very slightly tender. March 13, urine: no casts. March 20, urine: 1,016, albumen none, no casts. March 27, opening in shoulder almost healed. April 2, wound completely healed. Patient was discharged cured. Except for the difficulty in determining the opsonic index and for a delay in the preparation of a

vaccine, this patient would have been inoculated and his subsequent recovery would doubtless have been attributed to its use.

Case 4.—A. H. Female. 58. Dr. A. J. Bristow and Dr. W. H. Pratt, Brooklyn. February 25, rigors, fever, general muscular pains, intense headache. March 1, well. March 4, repetition of previous attack with more severe headache. March 10, well. March 11, tenderness over left side of neck. Fever, temperature  $100^{\circ}$  to  $103^{\circ}$ . March 17: moderately circumscribed swelling of left submaxillary triangle. No fluctuation. Leucocytes 15,000, polynuclears 78 per cent. March 18, swelling less painful, less tender. Leucocytes 12,000, polynuclears 78 per cent. March 20, swelling more diffuse, more painful. March 21, leucocytes 10,000, polynuclears 75 per cent. March 23, swelling had extended to clavicles, more tender. Leucocytes 11,000, polynuclears 83 per cent. A long incision parallel with anterior border of sternocleidomastoid, tissues much thickened and infiltrated. Deep in submaxillary fossa small abscess cavity opened, pus evacuated, drainage. Culture: *Strept. longus*

CHART 3.  
MRS. H. STREPTOCOCCUS ABSCESS IN NECK WITH MULTIPLE ARTHRITIS.  
Inoculated with streptococcus from A. R.



and a bacillus. March 24, edge of wounds glazed. Very little discharge. Urine: normal. March 26, intermittent pulse. March 27, severe pain in left leg. Some tenderness over internal condyle. March 28, infiltration of neck slowly disappearing. March 30, two slight convulsions limited to face and upper extremities, eyes to right. Face livid. Blowing murmur over mitral. March 31, pain in right knee and left forefinger and wrist. April 1, seen by Dr. Potter. Opsonic index to streptococcus A. R. (Dr. Krumwiede), 0.74. April 2, blood culture (Dr. N. E. Ditman) sterile. Inoculated with 25 millions streptococci A. R. (Vaccine prepared by Dr. Krumwiede.) April 4, wound diminished in size one-half. Joints have improved. Inoculated with 50 millions. April 11, wound practically healed. Convalescence uninterrupted. The striking features of this case are the improvement of the wound and joint symptoms within 48 hours after the first dose, and the sudden drop in the temperature and rapid improvement following within 48 hours after the sec-

ond inoculation and closely corresponding to the rise in the opsonic index, as plainly shown in the chart.

The question whether two sets of leucocytes give indices which are nearly alike (other conditions being the same) was investigated. The possibility of an altered power of phagocytosis in an infected person's leucocytes, was considered. In the later experiments the number of polynuclear neutrophiles (phagocytes) in the cream were counted as it was thought that the variations in the phagocytic average might coincide with the variations in the number of leucocytes. With fewer cells, other conditions being the same, one would expect more cocci to each cell. In other words, the phagocytic average would vary inversely as the number of leucocytes.

The following table shows our results and requires no explanation. Although no conclusions can be drawn from so few observations, especially when the results depend upon so inaccurate a method of technique, yet they seem to suggest, just as do similar observations upon the staphylococcus and the tubercle bacillus infections that the leucocytes of patients with pneumonia during the height of the disease are probably less active in phagocytic power than normal leucocytes. During and just after the crisis or lysis their phagocytic power increases rapidly, surpasses, and then later equals or becomes less than that of normal leucocytes.

MacDonald<sup>1</sup> in London examined 25 cases of acute croupous pneumonia and 17 cases of broncho-pneumonia. Although his figures are derived from many more experiments and show more striking variations, his results in the study of the opsonic index in pneumonia are practically the same as ours.

Wolf<sup>2</sup> in Chicago has also arrived at similar conclusions from the study of 11 pneumococcal infections, five of which were cases of typical lobar pneumonia terminating in crisis, two were fatal cases of pneumonia, two were migratory pneumonia and two were pneumonic empyema. He suggested the estimation of an antipneumococcal index by comparing the leucocytic index and the opsonic index and found this to be increased early in pneumonia, and to remain high until crisis was completed in cases with favorable terminations. Neither

<sup>1</sup> *Aberdeen University Studies*, No. 21, 1906.

<sup>2</sup> *Jour. Infect. Dis.*, 1906. 3. p. 731.

TABLE 1.

| CONDITION OF<br>PATIENT WHOSE LEUCOCYTES<br>WERE USED   | DATE    | PHAGOCYTIC<br>AVERAGE        |                              | RATIO<br>IN PER<br>CENT      | OPSONIC INDEX                   |                                 | SERUM                                                                             | NO. OF POLYNU-<br>CLEAR IN 1 C. MM.<br>OF LEUCOCYTIC<br>CREAM |          | RATIO<br>(IN-<br>VERSE)<br>PER<br>CENT | ORGANISM                    |
|---------------------------------------------------------|---------|------------------------------|------------------------------|------------------------------|---------------------------------|---------------------------------|-----------------------------------------------------------------------------------|---------------------------------------------------------------|----------|----------------------------------------|-----------------------------|
|                                                         |         | Normal<br>Leuco-<br>cytes    | Patient's<br>Leuco-<br>cytes |                              | Normal<br>Leuco-<br>cytes       | Patient's<br>Leuco-<br>cytes    |                                                                                   | Normal                                                        | Patients |                                        |                             |
| Lobar pneumonia 10th day ter-<br>minating empyema       | Feb. 5  | 2.26<br>1.06<br>2.37<br>2.11 | 1.17<br>1.05<br>0.81<br>0.94 | 0.52<br>0.54<br>0.34<br>0.45 | 0.94<br>.....<br>.....<br>..... | 1.20<br>.....<br>.....<br>..... | F. R. Pneum.<br>F. R. Pneum.<br>Normal<br>"                                       | .....                                                         | .....    | ....                                   | Pneum.<br>"<br>"            |
| Broncho-pneum. Convalescent                             | Feb. 19 | 3.57<br>2.04<br>2.84         | 2.31<br>2.03<br>1.96         | 0.66<br>0.69<br>0.70         | 1.25<br>1.03<br>.....           | 1.20<br>1.03<br>.....           | J. B. Pneum.<br>M. L. R. Pneum.<br>Normal                                         | .....                                                         | .....    | ....                                   | Pneum.<br>"                 |
| Streptococcus Septicopyemia                             | Feb. 23 | 1.69<br>1.40<br>1.80<br>1.65 | 1.13<br>0.92<br>1.10<br>1.24 | 0.67<br>0.61<br>0.66<br>0.75 | 1.02<br>0.90<br>1.09<br>.....   | 0.91<br>0.74<br>0.98<br>.....   | A. R. Sept. Pyem.<br>F. R. Pneum.<br>M. R. L. Pneum.<br>Normal                    | 16,107                                                        | 18,088   | 0.89                                   | Pneum.<br>"<br>"            |
| Same, extremely marked improve-<br>ment, temp. falling  | Mar. 5  | 4.61<br>4.02<br>3.70         | 5.97<br>7.90<br>4.64         | 1.30<br>1.61<br>1.25         | 1.24<br>1.33<br>.....           | 1.29<br>1.69<br>.....           | M. R. Pneum.<br>M. L. R. Pneum.<br>Normal                                         | 13,724                                                        | 12,853   | 1.06                                   | Pneum.<br>"                 |
| Same. Convalescent                                      | Mar. 25 | 1.43<br>1.33<br>5.31<br>5.24 | 1.85<br>1.80<br>4.68<br>4.58 | 1.26<br>1.35<br>0.88<br>0.87 | 1.07<br>.....<br>1.01<br>.....  | 1.02<br>.....<br>1.02<br>.....  | A. R. Sept. Pyem.<br>Normal<br>A. R. Sept. Pyem.<br>Normal                        | 11,850                                                        | 11,440   | 1.03                                   | Pneum.<br>"<br>Strep. A. R. |
| Lobar pneum. resolution, be-<br>ginning strep. pleurisy | Feb. 28 | 5.33<br>5.42<br>3.37<br>3.57 | 7.95<br>7.33<br>4.95<br>5.98 | 1.40<br>1.33<br>1.46<br>1.67 | 1.50<br>1.51<br>0.94<br>1.51    | 1.33<br>1.22<br>0.82<br>.....   | M. L. R. Pneum.<br>Q. R. Sept. Pyem.<br>M. R. Pneum.<br>Normal<br>M. L. R. Pneum. | 19,712                                                        | 24,825   | 0.79                                   | Pneum.<br>"<br>"            |
| Same. Cured                                             | Mar. 29 | 3.01<br>3.22                 | 3.06<br>3.34                 | 1.01<br>1.03                 | 0.93<br>.....                   | 0.91<br>.....                   | M. L. R. Pn + Pleur.<br>Normal                                                    | 9,940                                                         | 9,652    | 1.03                                   | Strep. M. L. R<br>Pneum.    |

of these two observers has noted the variability in the phagocytic power of leucocytes from patients with pneumococcal infections as compared with leucocytes from normal individuals.

NOTE.—Shortly before this article was put into type, my attention was called to Rosenow's studies upon the phagocytic power of pneumonic as compared with normal leucocytes (*Jour. Infect. Dis.*, 1906, 3, p. 683). These studies had escaped my notice. His observations were much more carefully conducted than ours, in that the leucocytes from each source were very thoroughly washed in normal saline and their numbers equalized in each cream. He does not state whether, as we did, he took into account the proportions of polymorphonuclears or not. His conclusions were that (1) pneumonic leucocytes are more resistant to heat than normal leucocytes; (2) when heated just sufficiently to lose their phagocytic power they are more positively chemiotactic; (3) they not only take up pneumococci which are freely susceptible to phagocytosis in large numbers, but take up strains that resist phagocytosis by normal leucocytes; (4) they are more actively phagocytic for certain rare strains of pneumococci in the absence of serum.

Our observations suggest a decreased phagocytic power before, and an increased during and after, the crisis. Rosenow, on the contrary, found an increased phagocytic power of all pneumonic leucocytes without reference to the stage of the disease or convalescence.